Spinal cord compression in a new homozygous variant of beta-thalassemia

Case report

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A patient is reported with a new genetic variant of beta-thalassemia, who suffered from a progressive partial transverse cord lesion caused by epidural hematopoietic tissue. He recovered after partial surgical removal of this tissue and subsequent radiotherapy.

KEY WORDS • spinal cord compression • extramedullary hematopoiesis • beta-thalassemia

Extramedullary hematopoiesis may occur in patients with disturbance of function of the blood-forming organs. The liver, spleen, and lymphatic tissue are usually involved, and localization in the spinal canal is rare. This mechanism of compensation in thalassemia has been reported previously. We have observed this rare complication in a patient with a new homozygous variant of beta-thalassemia.

Case Report

This 55-year-old man was referred to the neurosurgical department because of progressive weakness in the legs. He was known to have a new genetic variant of beta-thalassemia. On admission, he was no longer able to walk, and he had recently become completely incontinent.

Examination. The patient was pale and had yellow sclerae. There was no palpable lymphadenopathy. Heart and lungs were normal. Examination of the abdomen revealed scars of a splenectomy performed in 1952 and a cholecystectomy in 1980. The liver was palpable two finger breadths below the costal margin. Arterial pulsations in the abdomen, arms, and legs were normal. Souffles could not be heard. He had a severe but incomplete motor and sensory transverse cord lesion below T-8. There were brisk knee jerks and bilateral plantar extensor responses. The referring neurologist had already obtained cerebrospinal fluid (CSF) by lumbar puncture; CSF analysis showed a protein level of 749 mg%. Metrizamide (Amipaque), introduced by lateral cervical puncture, revealed a complete block at the T-5 level, probably due to extradural compression.

Laboratory tests on admission showed the following results: hemoglobin 8.2 mmol/liter; red blood cells 4.1 × 10^{12}/liter; mean corpuscular volume 104 femtoliters; mean corpuscular hemoglobin concentration 19.3 mmol/liter; reticulocyte count 410 × 10^9/liter; normoblasts 150/100 white blood cells (WBC); WBC 8.5 × 10^9/liter; erythrocyte sedimentation rate 12 mm in the first hour; serum bilirubin 43 µmol/liter; lactic dehydrogenase 314 mmol/liter. Howell Jolly bodies were seen in most red blood cells with one or two Heinz inclusions. Morphology of the erythrocytes showed variations in shape and size, but no microcytosis. Many target cells were seen. Staining with the Kleihauer-Bethke technique revealed resistant hemoglobin in all cells. Hemoglobin electrophoresis showed 98% hemoglobin F (Hb F) and 2% hemoglobin A2 (Hb A2). The leukocyte differential was within normal limits. An electrocardiogram and chest x-ray films were normal.

Operation. The spinous process of T-5 was identified by x-ray control shortly before the operation. The skin incision extended from T-4 to T-8. The bone of
Extramedullary compression in beta-thalassemia

Fig. 1. Left: Photomicrograph of the bone marrow smear. The hypercellularity mainly comprises nucleated erythroid cells. Right: Photomicrograph of a sample of surgically removed extradural tumor tissue. The appearance cannot be distinguished from that of bone marrow (left). Again, there is a predominance of erythroid cells, the presence of myeloid and lymphoid cells, and sparse megakaryocytes (not shown). May-Grünwald-Giemsa, × 500.

the T-5 spinous process was much softer than usual, and the bone marrow was dark purplish-blue in color. A sample of marrow was sent for microscopic examination. Removal of the arch of T-5 and the ligamenta flava revealed a dark blue tumor without a capsule. Soft tissue from this growth was also sent for microscopic examination. Removal of the tumor, which extended down the dorsal side of the cord from T-4 and T-8, caused extensive bleeding. Complete removal of the soft growth was impossible. A connection between the bone marrow of the spinous process and the tumor could not be established. At the end of the operation the dura pulsated normally.

Histopathological Examination. Pathological investigation of the tissue of the spinous process revealed hypercellular bone marrow. There was some disturbance in the myeloid-erythroid ratio, with a predominance of erythroid cells and discrete clusters of normoblasts and erythroblasts. Most of the erythrocytes had a nucleus. The specimen contained more maturing myeloid tissue and more megakaryocytes than normal (Fig. 1 left).

Tissue obtained from the tumor showed the same histopathological picture (Fig. 1 right). The diagnosis was extramedullary hematopoietic tissue and hypercellular bone marrow.

Postoperative Course. The postoperative neurological recovery was remarkable. A few days after surgery the patient could walk with the support of a cane, and 3 weeks later he walked without support. At that time, motor function and sensation were normal. The leg reflexes were still brisk, but the flexor responses were plantar. Control of bowel and bladder function was restored.

As the pathological extradural tissue had not been completely removed, radiotherapy (40 Gy total dose in 20 fractions) was administered from T-2 to T-9.

Discussion

A summary of reported cases of extramedullary hematopoietic tissue in patients with beta-thalassemia is presented in Table 1. Most patients suffer from heterozygous forms. The inheritable disorder, thalassemia, is normally only found in Negroes and in descendants of the original population of the Mediterranean area.

It is exceptional to find this disease in a purely Dutch family. Schokker, et al., described this family in 1966. In 1975, Luyendijk, et al., reported a homozygous case with spinal cord compression by hematopoietic tissue. Our patient is the first to be reported with a homozygous beta-thalassemia with a new genetic variant: Hb F 98%, Hb A2 2%.

In all cases reported so far, including our patient, the lesion has been located in the low to midthoracic region, probably because of the small diameter of the spinal canal in this area. The origin of hematopoietic tissue in the spinal canal remains uncertain. Lyall and Luyendijk, et al., have suggested a connection between the adjacent vertebral bone marrow and the hematopoietic tissue. Bree, et al., and Marinozzi reported an interrupted periosteum and vertebral cortex. Our operative findings do not support the assumption of a direct extension, because we were unable to establish a connection between the bone marrow and hematopoietic tissue. The course in our patient confirms the opinion expressed by others, that a good outcome can be obtained by laminectomy with removal of the tumor mass, followed by radiotherapy.

References

1. Appleby A, Batson GA, Lassman LP, et al: Spinal cord compression by extramedullary haematopoiesis in my-
TABLE 1
Summary of reported cases of beta-thalassemia with extramedullary hematopoietic tissue compressing the spinal cord

<table>
<thead>
<tr>
<th>Authors &amp; Year</th>
<th>Sex, Age (yrs)</th>
<th>Type of Thalassemia</th>
<th>Racial Group</th>
<th>Location</th>
<th>Therapy</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gatto, et al., 1954</td>
<td>M, 26</td>
<td>probably heterozygous</td>
<td>Italian</td>
<td>T5-10</td>
<td>surgery + radiotherapy</td>
<td>no marked improvement died</td>
</tr>
<tr>
<td>Marinozzi, 1958</td>
<td>F, 4</td>
<td>probably homozygous</td>
<td>Italian</td>
<td>T8-12, autopsy</td>
<td>none</td>
<td>good</td>
</tr>
<tr>
<td>Sorsdahl, et al., 1964</td>
<td>M, 40</td>
<td>probably homozygous</td>
<td>Negro, American</td>
<td>T5-8</td>
<td>surgery</td>
<td>good</td>
</tr>
<tr>
<td>Cauthen, et al., 1968</td>
<td>M, 47</td>
<td>probably homozygous</td>
<td>Negro, American</td>
<td>T4-8</td>
<td>surgery + radiotherapy</td>
<td>good</td>
</tr>
<tr>
<td>Heffner and Koehl, 1970</td>
<td>M, 21</td>
<td>probably homozygous</td>
<td>Italian</td>
<td>T8-L3, autopsy</td>
<td>none</td>
<td>died</td>
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<tr>
<td>Luyendijk, et al., 1975</td>
<td>M, 42</td>
<td>homozygous</td>
<td>Negro, Surinam</td>
<td>T5-7</td>
<td>surgery + radiotherapy</td>
<td>good</td>
</tr>
<tr>
<td>Cross, et al., 1977</td>
<td>M, 44</td>
<td>probably heterozygous</td>
<td>Negro, Jamaican</td>
<td>T-8</td>
<td>surgery + radiotherapy</td>
<td>good</td>
</tr>
<tr>
<td></td>
<td>F, 25</td>
<td>probably heterozygous</td>
<td>Negro, Jamaican</td>
<td>T-6</td>
<td>surgery + radiotherapy</td>
<td>good</td>
</tr>
<tr>
<td>Luitjes, et al., 1982</td>
<td>M, 55</td>
<td>homozygous, new variant</td>
<td>Dutch</td>
<td>T4-8</td>
<td>surgery + radiotherapy</td>
<td>good</td>
</tr>
</tbody>
</table>

References:

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